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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,291	NORRIS, MICHAEL CHRISTIAN	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-49 and 55-79* is/are pending in the application.

4a) Of the above claim(s) *42, 55-67, 72, 75, 76, 79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-41,43-49,68-71,73,74,77 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/16/2005, 7/31/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election of group I, claims 36-49, 68-74, 77 and 78 in the telephone interview (Sep 10 2008, Jun 5 2008) with traverse is acknowledged. Claims 42, 55-67, 72, 75, 76 and 79 are withdrawn from consideration. Claims 42 and 72 do not read on the opiate elected species codeine. Claims 1-35, 50-54 have been cancelled. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Thus the restriction requirement elected is made final. Claims 36-49, 55-79 are pending and claims 36-41, 43-49, 68-71, 73-74, 77 and 78 are being examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-38, 40, 41, 44-49, 68, 70-72, 74, 77, 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to a pharmaceutical composition comprising a combination of a selective or specific COX 2 inhibitor or a pharmaceutically acceptable salt or derivative thereof, an opiate or a pharmaceutically acceptable salt or derivative thereof, and a centrally-acting cyclo-oxygenase inhibitor or a pharmaceutically acceptable salt or derivative thereof, as active ingredients, and a pharmaceutically acceptable carrier. The claims are unclear as to "derivative". The broadest reasonable interpretation of derivatives of a compound

covers all future improvements without regard to whether Applicants invented such improvements, which would undermine the function of the claims because it would allow Applicants to benefit from the ambiguity, rather than requiring Applicants to give proper notice of the scope of the claims to competitors. Additionally, adopting the broadest reasonable construction of the claims could retard innovation because cautious competitors may steer too far around that which Applicants actually invented, neglecting improvements that otherwise might be made. See *Halliburton Energy Services Inc. v. M-I LLC*, 85 USPQ2d 1654 (Fed. Cir. 2008). Accordingly, the metes and bounds of the claims are not clearly set forth and the scope of the invention cannot be distinctly ascertained.

Claims 36, 44, 45, 47, 74, 77, 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation of "sub-therapeutic amounts" is ambiguous in each of the rejected claims because the entire recitation appears relative. Accordingly, the metes and bound of this limitation and subsequently the claims are not clear. The specification also fails to clearly define what the intended amount for each drug to be protected. It is not clear whether this language is directed to a lower individual or bolus doses, a lower number of frequencies etc. A therapeutic amount of either COX-2 inhibitor or an opiate or a cyclo-oxygenase inhibitor is viewed as any amount that can at least to some degree alleviate the pain. Accordingly, a "subtherapeutic amount" is relative in relationship to the ultimate clinical

outcome sought. Therefore, Examiner views such limitation to be relative and thus ambiguous.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 36, 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaiko et al. (U.S. 6,277,384).

Kaiko et al. teaches oral dosage forms comprising an opioid analgesic and acetaminophen and cox-2 inhibitor and mixtures thereof (p 34 claim 1 and p 35 claim 7). Thus Kaiko's teachings anticipated the claimed invention of a pharmaceutical composition comprising a combination of a COX-2 inhibitor, an opiate and a cyclo-oxygenase inhibitor.

Claims 36, 38, 39, 45, 68, 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaiko et al. (U.S. 6,375,957).

Kaiko et al. teaches oral dosage forms comprising an opioid analgesic such as codeine and acetaminophen and cox-2 inhibitor and mixtures thereof (claims 1, 6, 32, 34 and 44). Thus Kaiko's teachings anticipated the claimed invention of a pharmaceutical composition comprising a combination of a COX-2 inhibitor, an opiate and a cyclo-oxygenase inhibitor.

Note: The above references drawn to a non-elected species with regard to the COX-2 inhibitor was found during the search for the elected species. It should not be interpreted that a comprehensive search was performed for all non-elected species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 36-41, 43-49, 68-71, 73-74, 77 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaiko et al. (U.S. 6,375,957) in view of Bennett et al. (Expert Opin Pharmacother 2001, 2(11) 1859-76).

Kaiko et al. teaches the compositions comprising combination of acetaminophen, opioid analgesic and COX-2 inhibitor (col. 39, claim 1 and col. 42, claim 44). The reference teaches compositions comprising acetaminophen and opioid analgesic are useful in a method of treating pain (col. 5, lines 10-14). The reference teaches the combination of acetaminophen and codeine, opioid analgesic composition are

commercially available and typical oral capsule dosages of acetaminophen/codeine combinations include 325 mg of acetaminophen and 15 mg of codeine phosphate (col 15, lines 7-20). The reference teaches that lower doses of the opioid analgesic or acetaminophen (apparent one-way synergy), or lower doses of both drugs (two-way synergy) than would normally be required when either drug is used alone can be combined and further teach that by using lower amounts of either or both drugs, the side effects associated with effective pain management in humans are significantly reduced (col. 15, lines 50-56). Kaiko et al. teaches in one of the embodiments a pharmaceutical composition comprising an analgesically effective dose of an opioid analgesic together with a dose of acetaminophen effective to augment the analgesic effect of the opioid analgesic, i.e., the dose of opioid potentiates the effect of the acetaminophen (col. 16, lines 3-7). The reference teaches that additional non-opioid agents may be included in the formulations of opioid agonist/opioid antagonist, or combinations of opioid agonist/opioid antagonist/acetaminophen which agents may or may not provide additive, synergistic (superadditive) effects and allows for the use of lower doses of the opioid analgesic by virtue of the inclusion of an additional non-opioid agonist, such as an NSAID or a COX-2 inhibitor and may provide additional analgesic effect (col. 17, lines 20-40). The reference further teaches that by using lower amounts of either or both drugs, the side effects associated with effective pain management in humans are reduced (col. 17, lines 42-52). The reference teaches meloxicam (elected COX-2 inhibitor species) as COX-2 inhibitor and further discusses the therapeutic

dosage that will be effective in combination with an opioid analgesic (col. 18, line 46, lines 49-55).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have formulated a pharmaceutical composition comprising a combination of a selective COX-2 inhibitor such as meloxicam (elected species), codeine (elected opiate) and a cyclo-oxygenase inhibitor such as paracetamol (elected species) because of the teachings of Kaiko et al. Kaiko et al. teaches an oral dosage form comprising an opioid analgesic, acetaminophen and a cox-2 inhibitor. The reference teaches that codeine-acetaminophen (acetaminophen is paracetamol) combination is commercially available and also teaches such combinations with different dosage amounts of the drugs and further teach that COX-2 inhibitor such as meloxicam can be added to provide additional analgesia. One having ordinary skill in the art would have been motivated to formulate a composition comprising meloxicam, codeine and paracetamol because of expectation of success as paracetamol- codeine combination is known and also to provide additional analgesia as taught by Kaiko et al. One of ordinary skill in the art would have been motivated to incorporate the three agents herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat pain individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows

logically from their having been used individually in the prior art. *In reSussman,* 1943 C.D. 518; *In re Pinten,* 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi,* 58 CCPA 1074, 1079-80; 440 F.2d 442,445; 169 USPQ 423, 426 (1971); *In reCrockett,* 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). Thus, since the individual components are known to be used individually in the art for the same purpose, then to use them together in one composition is obvious.

Kaiko et al. does not explicitly teach that the pain is associated with inflammation or associated with trauma, osteoarthritis etc as claimed in claims 48 and 49.

Bennett teaches COX-2 inhibitors as non-steroidal anti-inflammatory drugs and further teach their therapeutic effectiveness in osteoarthritis (see Abstract and Table 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention the pharmaceutical composition comprising a COX-2 inhibitor such as meloxicam to be useful in a method of treating pain associated with inflammation or associated with a condition such as osteoarthritis from the teachings of Bennett et al as the reference teaches the cox-2 inhibitor compounds as anti-inflammatory agents and also teach their usefulness in osteoarthritis.

** Please note that the recitation of "intended use", e.g., treating pain associated with inflammation or associated with trauma, osteoarthritis etc does not lend patentable weight to composition claims.

Claims 36-41, 43-49, 68-71, 73-74, 77 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cooper (U.S. 6,924,303) in view of Kaiko et al. (U.S.

6,375,957) and further in view of Bennett et al. (Expert Opin Pharmacother 2001, 2(11) 1859-76).

Cooper teaches pharmaceutical compositions which consists essentially of a cyclooxygenase-2 inhibitor and a compound selected from the group consisting of non-steroidal anti-inflammatory drugs, acetaminophen and mixtures thereof (see Abstract) to alleviating pain and or inflammation (col.1, lines 10-12). The reference teaches that the cyclooxygenase-2 inhibitor such as meloxicam must be present in an analgesia-inducing amount and/or pain-alleviating amount (col.4, lines 21-23). The reference teaches that cyclooxygenase-1 inhibitor such as acetaminophen must be present in an analgesia-inducing or pain-alleviating amount (col.4, lines 38-40, col. 5, lines 14-19).

The reference does not teach opiate in the composition.

Kaiko et al. teachings discussed as above. Kaiko et al. teach a pharmaceutical composition comprising an opiate agonist such as codeine with paracetamol. The reference teaches that additional non-opioid agents may be included in the formulations of opioid agonist/opioid antagonist, or combinations of opioid agonist/opioid antagonist/acetaminophen, such as an NSAID or a COX-2 inhibitor that may provide additional analgesic effect (col. 17, lines 20-40).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have formulated a composition comprising meloxicam, acetaminophen (paracetamol) and an opiate because of the teachings of Cooper and Kaiko. Cooper teaches a pharmaceutical composition comprising a cox-2 inhibitor such as meloxicam and acetaminophen and Kaiko teaches that a cox-2 inhibitor can be formulated in

combination with an opiate such as codeine and acetaminophen. One having ordinary skill in the art at the time of the invention would have been motivated to combine all the three drugs in a single pharmaceutical composition in expectation of success, to provide additional analgesic effects and in providing synergistic or additive therapeutic benefits in relieving pain. One of ordinary skill in the art would have been motivated to incorporate the three agents herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat pain individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In reSussman,* 1943 C.D. 518; *In re Pinten,* 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); *Inre Susi,* 58 CCPA 1074, 1079-80; 440 F.2d 442,445; 169 USPQ 423, 426 (1971); *In reCrockett,* 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). Thus, since the individual components are known to be used individually in the art for the same purpose, then to use them together in one composition is obvious.

The references do not explicitly teach that the pain is associated with trauma, osteoarthritis etc as claimed in claims 48 and 49.

Bennett teaches COX-2 inhibitors as non-steroidal anti-inflammatory drugs and further teach their therapeutic effectiveness in osteoarthritis (see Abstract and Table 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention the pharmaceutical composition comprising a COX-2 inhibitor such as meloxicam to be useful in a method of treating pain associated with a condition such as osteoarthritis from the teachings of Bennett et al as the reference teaches the cox-2 inhibitor compounds as anti-inflammatory agents and also teach their usefulness in osteoarthritis.

** Please note that the recitation of "intended use", e.g., treating pain associated with inflammation or associated with trauma, osteoarthritis etc does not lend patentable weight to composition claims.

Claims 36-41, 43-49, 68-71, 73-74, 77 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cooper (U.S. 6,924,303) in view of Burch et al. (U.S. 6,552,031).

Cooper's teachings discussed as above. Cooper teaches pharmaceutical compositions which consists essentially of a cyclooxygenase-2 inhibitor and acetaminophen (see Abstract) to alleviating pain and or inflammation (col.1, lines 10-12).

The reference does not teach opiate in the composition.

Burch et al. teaches pharmaceutical compositions comprising COX-2 inhibitors with opioid analgesics such as codeine, hydrocodone etc. The reference teaches meloxicam as one of the COX-2 inhibitors. The reference teaches a composition comprising meloxicam and morphine (example 2). The reference teaches codeine as one of opiates that can be formulated with a COX-2 inhibitor. The reference teaches

that in certain preferred embodiments, the invention is directed to pharmaceutical formulations comprising a COX-2 inhibitor in an amount sufficient to render a therapeutic effect together with a dose of codeine which is analgetic if administered without the COX-2 inhibitor (col.6, lines 22-28). The reference further relates to the use of a pharmaceutical combination of a COX-2 inhibitor together with an opioid analgesic to provide effective pain management in humans (Col.6, lines 62-65). Burch et al. teaches that the compositions comprising a COX-2 inhibitor and an opioid analgesic can be used in obtaining relief from moderate to severe pain with or without inflammation and in conditions such as arthritis, including rheumatoid arthritis, degenerative joint diseases (osteoarthritis) etc. (col. 15, lines 48-50, 67, col. 16, lines 4-5).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have formulated a composition comprising meloxicam, acetaminophen (paracetamol) and an opiate because of the teachings of Cooper and Burch et al. Cooper teaches a pharmaceutical composition comprising a cox-2 inhibitor such as meloxicam and acetaminophen and Burch et al. teaches pharmaceutical composition comprising a cox-2 inhibitor with an opiate such as codeine. Burch et al. teaches a composition comprising meloxicam and morphine (example 2). One having ordinary skill in the art at the time of the invention would have been motivated to combine all the three drugs in a single pharmaceutical composition in expectation of success, to provide additional analgesic effects and in providing synergistic or additive therapeutic benefits in relieving pain. One of ordinary skill in the art would have been motivated to incorporate the three agents herein in a single combination pharmaceutical composition

because combining the agents herein each of which is known to be useful to treat pain individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In reSussman,* 1943 C.D. 518; *In re Pinten,* 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); *Inre Susi,* 58 CCPA 1074, 1079-80; 440 F.2d 442,445; 169 USPQ 423, 426 (1971); *In reCrockett,* 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). Thus, since the individual components are known to be used individually in the art for the same purpose, then to use them together in one composition is obvious.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to UMAMAHESWARI RAMACHANDRAN whose telephone number is (571)272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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